

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

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PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2004/050901

International filing date (day/month/year)  
14.06.2004

Priority date (day/month/year)  
16.06.2003

International Patent Classification (IPC) or both national classification and IPC  
A61K31/155, A61K9/20, A61K9/00, A61K9/16, A61P3/08

Applicant  
RANBAXY LABORATORIES LIMITED

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**1. This opinion contains indications relating to the following items:**

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

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INTERNATIONAL SEARCHING AUTHORITYInternational application No.  
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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material:
    - in written format
    - in computer readable form
  - c. time of filing/furnishing:
    - contained in the international application as filed.
    - filed together with the international application in computer readable form.
    - furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. II Priority**

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1.  The following document has not been furnished:

copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).  
 translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2.  This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
- claims Nos. 60, 61 (industrial applicability)

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the whole application or for said claims Nos. 60, 61 (industrial applicability)
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes:	Claims	20-40
	No:	Claims	1-19, 41-61
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-61
Industrial applicability (IA)	Yes:	Claims	1-59; for 60 and 61 see separate sheet
	No:	Claims	

**2. Citations and explanations**

**see separate sheet**

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claims 60 and 61 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

2. Reference is made to the following documents:
  - D1: US 2003/104059 A1 (CHAWLA MANISH ET AL) 5 June 2003
  - D2: WO 02/28181 A (TEWARI PRASHANT KUMAR ; USV LTD (IN); GIDWANI SURESH KUMAR (IN); SINGN) 11 April 2002
  - D3: US-A-6 117 451 (KUMAR VIJAI) 12 September 2000
  - D4: US-A-5 955 106 (GABEL ROLF-DIETER ET AL) 21 September 1999
  - D5: WO 03/026637 A (REDDY HARIVARDHAN L ; TYEBJI ZIAUDDIN Z (IN); SUN PHARMACEUTICAL IND L) 3 April 2003
  - D6: US 2003/104049 A1 (SHERMAN BERNARD CHARLES) 5 June 2003
  - D7: WO 03/028704 A (ARORA VINOD KUMAR ; MALIK RAJIV (IN); MADAN ASHISH (IN); MURPANI DEEPA) 10 April 2003

If not indicated otherwise, the relevant passages are those mentioned in the International Search Report.

3. The present application according to **claim 1** relates to an extended-release metformin tablet, comprising: a) from about 500 mg to about 1000 mg metformin, b) 5-25% w/w rate-controlling polymer(s), and c) other pharmaceutically acceptable excipients; in **claim 41** the tablet is monolithic. **Claim 20** is directed to a process for preparing extended-release metformin tablets, comprising: a) blending metformin, 5-25 % w/w rate-controlling polymers and other pharmaceutically acceptable excipients, b) compacting/slugging, c) milling or crushing the compacted/slugged material of step b) into granules, and d) lubricating and compressing the granules to form tablets.

Finally, **claim 60** relates to a method for the treatment of non-insulin dependent diabetes mellitus comprising administering said extended-release metformin tablets.

- 4.1. The present application does not meet the requirements of the PCT with respect to novelty (Art. 33(2)) for the following reasons. **D1**, **D2**, **D3**, **D4**, **D5**, and **D6** all disclose controlled-release tablets containing metformin which fall within the terms of present claims 1 and 41, whereby these documents are novelty destroying for at least independent claims 1, 41 and 60.
- 4.2. However, the process according to present **claim 20** is novel over the prior art.
5. No inventive step can be recognised for those claims whose subject-matter is not novel. Furthermore, the process according to present **claim 20** does not involve an inventive step (Art. 33(3) PCT) for the following reasons.

**D7** is regarded as the most relevant prior art document for claim 20. It discloses a method to produce controlled-release tablets containing metformin which includes a step of moisture conditioning followed by the blending of the mixture. The blended mixture is then compacted or slugged, milled or crushed into granules, and finally lubricated and compressed. The method according to present claim 20 differs in that the content of the rate-controlling polymer is specifically 5-25 %, this is lower than those used in the specific examples of **D7**.

Thus, the problem to be solved by the present application is regarded in the provision of alternative processes controlled-release tablets containing metformin. The solution provided by the present application is regarded as an obvious alternative to that disclosed in **D7**. Decreasing the relative content of the rate-controlling polymer with respect to those used in the specific examples of **D7** during the blending step represents a minimal change which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages achieved can readily be foreseen. Furthermore, **D7** discloses a range for the rate controlling polymer of 10-60 % (see page 5, lines 9-10). Consequently, no inventive step is recognised.

- 6.1. Claims 1-59 meet the criterion set forth in Article 33(4) PCT because their subject-matter is susceptible of industrial application.

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6.2. For the assessment of the present claims 60 and 61 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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